Falls in Rheumatoid Patients: Does Ankle and Foot Ultrasonography have a Predictive Role? A Single-blind Study

Stürze bei Patienten mit rheumatoider Arthritis: Hat die Sonographie am Knöchel und Fuß einen Vorhersagewert? Eine Einfachblindstudie

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ABSTRACT

Background Rheumatoid arthritis (RA) patients have a higher prevalence of falls compared with the healthy population. Several risk factors of falls in RA have been postulated, including high disease activity, low balance, muscle weakness and non-treatment with biologics.

Aim of the work We investigated our hypothesis that the sonographically detected ankle and foot changes in RA patients can predict falls in this population. To our knowledge, no previous study had investigated this before.

Methods In a total of 101 RA patients, we performed assessments of disease activity, disability level, gait speed, balance status, clinical examination of ankle and foot and an MSUS assessment of the ankle and foot joints and tendons as possible risk factors of falls.

Results The Berg balance test had the highest fall-predicting power (71.3 %), followed by a gait speed test and restricted range of motion (ROM) of the Rt. subtalar joint, each with a predictive power of 70.3 %. Of the sonographic findings, erosion of the first metatarsophalangeal (MTP) joint was the most accurate fall predictor, followed by erosion of the talonavicular joint and tenosynovitis of the ankle dorsal flexors with an area under the curve of 0.656, 0.642 and 0.614, respectively.

Conclusion The use of the MSUS as an adjunct objective method for predicting falls in RA patients has not been studied before. It was found that clinical foot and balance testing was a superior and easier way of predicting falls in RA patients than using ultrasonography.

ZUSAMMENFASSUNG

Hintergrund Bei Patienten mit rheumatoider Arthritis (RA) ist die Prävalenz von Stürzen im Vergleich zur gesunden Bevölkerung erhöht. Für Stürze bei RA wurden mehrere Risikofaktoren postuliert, darunter hohe Krankheitsaktivität, Gang- und Standunsicherheit, Muskelschwäche und Nichtbehandlung mit Biologika.

Ziel der Arbeit Wir untersuchten unsere Hypothese, dass sonographisch nachgewiesene Veränderungen an Knöcheln und Füßen bei RA-Patienten Stürze in dieser Population vorhersagen können. Nach unserem Kenntnisstand wurde dies noch nicht in einer früheren Studie untersucht.

Methoden Bei insgesamt 101 RA-Patienten erfolgten eine Beurteilung der Krankheitsaktivität, des Behinderungsgrads, der Ganggeschwindigkeit, der Gang- und Standsicherheit sowie eine klinische Untersuchung der Knöchel und Füße und eine MSUS-Untersuchung der Knöchel, Füße und Sehnen im Hinblick auf mögliche Risikofaktoren für Stürze.

Ergebnisse Der Berg-Gleichgewichtstest hatte die höchste Vorhersagekraft für Stürze (71,3 %), gefolgt von einem Gang-

geschwindigkeitstest und einem eingeschränkten Bewegungsumfang (ROM) des rechten Subtalargelenks, jeweils mit einer Vorhersagekraft von 70,3 %. Von den sonographischen Befunden war die Erosion des ersten Metatarsophalangealgelenks (MTP) der genaueste Sturzprädiktor, gefolgt von der Erosion des Talonavikulargelenks und der Tenosynovitis der Knöcheldorsalflexoren, mit einer Fläche unter der Kurve von 0,656, 0,642 bzw. 0,614.

Schlussfolgerung Die Verwendung des MSUS als zusätzliches objektives Verfahren zur Vorhersage von Stürzen bei RA-Patienten wurde bislang noch nicht untersucht. Unsere Studie ergab, dass die klinische Untersuchung des Fußes und der Gang- und Standsicherheit eine überlegene und einfachere Methode zur Vorhersage von Stürzen bei RA-Patienten ist als die Verwendung von Ultraschall.

Introduction

Falling is a major public problem with major health and economic consequences. Although it was extensively studied in elderly population in whom falls occur in around 30 % [1], Rheumatoid arthritis (RA) patients have higher prevalence of falls compared to the healthy population [2]. Fall is a multifactorial event with interaction between internal and external factors [3, 4]. Several fall risk factors were diagnosed in RA; including muscle weakness, joint pain , joint deformity, fatigue, defected balance and gait problems [2].

Prediction of falls in RA is of a paramount importance where it allows early application of fall preventive measures and protects the patient from painful disabling experiences including fractures and traumatic brain injuries. Among the factors previously studied as fall predictors in RA were muscle volume, balance status, functional performance and functional disabilities [3, 4].

Although the feet and ankle joints are commonly affected in RA patients, clinical assessment is usually neglected in routine care. Postulated causes include the exclusion of ankle and foot examination from the DAS-28 score which is a common tool for patients' follow up and the presence of foot deformities that hinder proper examination [5].

Musculoskeletal ultrasonography can detect subclinical inflammation and structural damage and helps in the follow up process. Besides being is a bedside, relatively cheap, radiation free tool with diagnostic efficacy comparable to MRI [6].

As far as we can tell, no previous study used the MSUS detected ankle and foot changes as predictor of falls in patients with RA. Therefore, in this study we aimed to investigate our hypothesis claiming that sonographic examination of ankle and foot can predict fall risk in RA patients.

Subjects and methods

Study design and study setting This is an observational cross section study that was conducted in the outpatient clinic and inpatient word of the Rheumatology and Rehabilitation Department of our university hospital.

Ethical Consideration This study was approved by the local ethical committee of the Faculty of Medicine and according to the declaration of Helsinki. Clinical trial registration ID (NCT04464096). All patients provided written informed consent before enrollment.

Patients Eligible patients were 101 adult RA patients fulfilling the 2010 ACR/EULAR criteria [7] who were consecutively presented at the outpatient clinic and inpatient word of the Rheumatology department during a 12 months period from April 2018 to April 2019.

Exclusion criteria were patients aged <18 years or those using walking assistive devices, those with lower limb disability preventing the participant from performing the mobility tests, and those who were using antidepressants and/or sedatives. Patients with severe comorbidities, severe vision impairment, hearing loss or neurological diseases that interferes with the mobility as stroke or neuropathy, were also excluded.

Methods

Basic demographic and clinical data were collected including age, sex, family history and disease duration. History of chronic foot pain of >3 months and current medication history were also recorded. All participants were examined clinically for systemic and musculoskeletal evaluation. Each patient was assessed for disease activity using Disease activity score (DAS 28) ESR [8] and functional level using Health assessment questionnaire disability index (HAQ-DI) score [9]. History of falling defined as "an unexpected event in which the person comes to rest on the ground, the floor or lower level" [10] in the past year was taken and accordingly, patients were divided into fallers and non-fallers. Foot problems were assessed clinically by manual muscle power testing of the muscles around the ankle joint and subtalar joint [11]. Muscle power of the toes was assessed by the paper grip test [12]. Plantar sensation was assessed at 6 sites using a 10-gm monofilament (fine touch) [13]. Assessment of the range of motion of ankle joint was done using a modified lunge test [14] and passive subtalar ROM was performed clinically . According to foot type examination using the wet test technique [15], 3 types of feet were diagnosed; normal Arch foot, flat foot and high Arch foot. Foot deformities were assessed clinically by inspecting and palpating the feet in setting and standing positions .Patients' balance status were investigated using the Berg balance scale (BBS) [16] and Tenitti balance assessment tool (TBAT) [17]. Gait speed (self-selected)was assessed using 6-meters walk test [18]. The physical examination and clinical tests were performed by a rheumatologist who was blind to the fall history of the patients.

Laboratory investigations including complete blood count (CBC), erythrocyte sedimentation rate (ESR), liver and renal function test and Rheumatoid factor (RF) were performed to the studied patients.

Musculoskeletal ultrasonography (MSUS) of foot and ankle
Using a high end machine; MyLab 7 (Esaote, Europe B.V. Maastricht, Netherlands) with high frequency linear array transducer (10–19 MHz). Four joints were assessed bilaterally for synovial proliferation and synovitis by grey scale (GS) and power Doppler (PD) modes. In each foot; tibiotalar, talonavicular and metatarsophalangeal joints (first and second) were examined. Tendons around the ankle (dorsal flexors, plantar flexors and peroneal tendons) were examined for tenosynovitis by GS and PD. The following variables were measured on each evaluation:

Synovitis (19)*:* which is hypoechoic thickening with or without effusion with 4 grades, *Doppler activity*[19]: After adjustment of the machine to get the power Doppler mode, 4 grades PD are prescribed; Grade 0 to 3, *Tenosynovitis*(20)*:* Defined as a hypoechoic or anechoic thickened tissue with or without fluid within the tendon sheath. Tenosynovitis was evaluated and graded by grey scale(GS) and power Doppler (PD) using qualitative score, binary evaluation – 0 (absent) or 1 (present), *Bone erosion*[20]: Erosion was defined as an interruption of the bone surface on two perpendicular planes. Semi-quantitative scoring of bone erosion: Grade 0 to 3 [21] was used.

The MSUS examination was done by a rheumatologist with 6 years' experience in MSUS, and who was blind to the fall history and clinical data of the patient.

Statistical analysis

Data were verified, coded by the researcher, and analyzed using SPSS version 21. Descriptive statistics: Means, standard deviations, medians, inter-quartile range (IQR) and percentages were calculated. Test of significances: Chi square and Fisher Exact tests were used to compare the difference in distribution of frequencies among different groups. For continuous variables, independent t-test analysis was carried out to compare the means of normally distributed data, while Mann-Whitney U test was calculated to test the median differences of the data that do not follow normal distribution. Multivariate logistic regression analysis was calculated to investigate the significant factors influencing falling history (Odds Ratio -OR- and 95 % confidence interval – 95 % CI). The clinical and demographic and sonographic factors with proven statistical significance from the univariate analyses were further included in the multivariate models. ROC curve was depicted for the predictive performance of the different correlates of falling, analyzed as area under the curve (AUC), standard error (SE) and 95 % CI. Validity statistics (sensitivity, specificity, positive and negative predictive value –PPV & NPV-) were calculated. A p-value equals or less than 0.05 was considered significant

Results

One hundred eight patients were found to be eligible for the study. Seven patients were excluded; three patients refused to participate in the study, while four patients missed the MSUS appointment.

According to the falling history within the last year, 101 RA patients were grouped into fallers (45 patients) and non-fallers (56 patients). The frequency of falling accidents in the fallers were as following, only once in 31 (68.9 %) patients, twice in 11 (24.4) three times and more in 3 (6.7 %). Falling resulted in bone fracture in 4 (8.9 %) patients, Minor head trauma in 3(6.7 %) and only bruising in the rest of patient (84.4 %).

▶ **Table 1** shows the basic demographic and clinical data of the patients. We found that 73.2 % of non-fallers had moderate disease activity while 60 % of fallers had high disease activity.

Around 80 % of fallers were at moderate and high risks of fall according to both Tinetti and Berg balance tests while nearly 60 % in non-fallers were at low fall risk.

Physical examination of the ankles and feet of the studied population were shown in ▶ **Table 2** which reviled that feet of the fallers showed weaker muscles of the ankle, subtalar and toes and more restricted ROM of the ankle and subtalar joints compared to the non- fallers' feet with significant differences between them ($P < 0.05$). Most of non-fallers (91.1 %) were having normal medial longitudinal arch compared to 60 % in fallers' feet with highly significant difference between them ($P = 0.001$). Hammer toe deformity was the commonest deformity in both fallers and non-fallers; 48.9 and 25 % respectively. Normal plantar sensation was detected in all our patients.

Ankle and foot MSUS examination of our study population by both GS and PD showed variable degrees of both inflammatory and destruction changes at the level of the joints and the surrounding tendons. Synovial hypertrophy, erosion and effusion of the examined joints and tenosynovitis of the surrounding tendons were detected. Synovial hypertrophy of the TNJ was the commonest joint finding while tenosynovitis of the peroneal muscles was the commonest ultra-sonographic finding on the level of tendons ▶ **Table 3**.

Significant differences were found between fallers and non- fallers as regards erosions at the Rt. ankle joint, Lt. talonavicular joint and Lt 1st and 2nd MTP joint. P value (0.025, 0.037, 0.020 and 0.006) respectively. Berg balance test had the most fall predicting power (71.3 %), followed by gait speed test and restricted ROM of the Rt. Subtalar joint with predictive power of 70.3 % both ▶ **Table 4**.

▶ **Table 5** shows that among all the defined predictors of fall, the most accurate predictors were Berg balance test, Tenitti balance test and gait speed test with area under the curve (0.786, 0.778 and 0.748) respectively. On the other hand, of all the sonographic findings, erosion of the 1st MTP joint was the most accurate predictor of fall followed by erosion of the Talonavicular joint and tenosynovitis of the ankle dorsal flexors(extensors) with area under curve (AUC) of 0.656, 0.642 and 0.614 respectively ▶ **Fig. 1**.

Discussion

Falling is a global problem with multiple health and economic consequences. Compared to healthy population, rheumatoid patients were found to have a higher fall risk [22]. Among the adverse effects of falling in Rheumatoid population are the reduction in the quality of life in addition to increased rates of morbidity and mortality [23].

Although the use of MSUS in detecting foot pathology was suggested as a predictor of patient reported foot related future disability [24], sonographic examination of RA patients concentrated on assessing wrist and hand joints with very few studies [25, 26] investigated the feet and ankles, generally on symptomatic ones.

▶ **Table 1** Demographic and Clinical Characteristics of the Studied Groups.

Variable	Non-Fallers (N = 56)	Fallers (N = 45)	P-value
Age/Years	45.21 ± 11.4	50.56 ± 12.8	0.029 *
Sex (Male/Female)	4/52	4/41	0.514 **
Disease Duration/ Years mean ± SD	5.87 ± 0.8	7.72 ± 1.2	0.001 *
Disease Duration (Early/Late)	12/44	5/40	0.133 **
ESR 1st hour mean ± SD	41.82 ± 2.8	45.96 ± 3.4	0.164 *
Positive RF N (%)	35 (62.5 %)	29 (64.4 %)	0.503 **
Disease Activity (DAS-28) N (%)			
▪ High Activity	12 (21.4 %)	18 (60 %)	0.029 **
▪ Moderate Activity	41 (73.2 %)	27 (40 %)	
▪ Mild Activity	3(5.4 %)	0	
▪ Remission	0	0	
Gait Speed Test (Median, IQR)	1.2 (0.6)	0.7 (0.5)	< 0.001 *
HAQ-DI (Median, IQR)	1.2 (0.8)	1.7 (0.9)	0.009 *
HAQ-DI Severity Category			
▪ Mild to Moderate Disability	27 (48.2 %)	14 (31.1 %)	0.082 **
▪ Moderate to Severe Disability	29 (51.8 %)	31 (68.9 %)	
Tinetti balance Assessment	24 (3)	20 (10)	< 0.001 *
Tinetti Severity Category			
▪ Low fall Risk	34 (60.7 %)	9 (20 %)	< 0.001 **
▪ Moderate fall Risk	22 (39.3 %)	19 (42.2 %)	
▪ High fall Risk	0 (0 %)	17 (37.8 %)	
Berg balance scale (Median, IQR)	37.5 (17)	40 (13)	0.044 *
Berg balance Category			
▪ Low fall Risk	32 (57.1 %)	8 (17.8 %)	< 0.001 **
▪ Medium fall Risk	22 (39.3 %)	19 (42.2 %)	
▪ High fall Risk	2 (3.6 %)	18 (40 %)	

* Independent t-test was used to compare the means among groups. ** Chi-square analysis was used to compare the frequency among groups. N: number, ESR: Erythrocyte sedimentation rate, DAS-28: Disease Activity Score-28, Significance was considered when P value is ≤ 0.05.

▶ **Table 2** Clinical foot Characteristics of the Studied Groups.

Variable	Non- fallers (N = 56)	Fallers (N = 45)	P-value
Weak Muscle Power N (%)			
Rt. Ankle J (dorsiflexors & plantar flexors)	4 (7.1 %)	17 (37.8 %)	< 0.001 **
Rt. Subtalar J (Ever & Inver)	5 (8.9 %)	16 (35.5 %)	0.001 **
Lt. Ankle J (dorsiflexors & plantar flexors)	6 (10.7 %)	13 (28.9 %)	0.020 **
Lt. Subtalar (Ever & Inver)	5 (8.9 %)	13 (28.9 %)	0.009 **
weak Toe Strength	5 (8.9 %)	17 (37.8 %)	0.001 **
Restricted ROM N (%)			
Rt Ankle	6 (10.7 %)	19 (42.2 %)	< 0.001 **
Rt Subtalar	4 (7.1 %)	19 (42.2 %)	< 0.001 **
Lt Ankle	8 (14.3 %)	19 (42.2 %)	0.002 **
Lt Subtalar	3 (5.4 %)	15 (33.3 %)	< 0.001 **
Foot Type N (%)			
Normal	51 (91.1 %)	27 (60 %)	0.001 *
Flat foot	3 (5.4 %)	9 (20 %)	
High Arched Foot	2 (3.5 %)	9 (20 %)	
Ankle & Foot Deformity N (%)			
Pronated foot	1 (1.8 %)	2 (4.4 %)	0.418 **
Dislocated Toe Joint	0 (0 %)	4 (8.9 %)	0.036 **
Hammer Toe	14 (25 %)	22 (48.9 %)	0.013 *
Hallux Valgus	1 (1.8 %)	3 (6.7 %)	0.211 **

* Independent t-test was used to compare the means among groups. ** Chi-square analysis was used to compare the frequency among groups. N: number, Rt: right, Lt: left, Ever: evertors, Inver: invertors, ROM: range of motion; Significance was considered when P value is ≤ 0.05.

In our study, 44.6 % of the studied patients gave positive history of falling within the last year. This was in agreement with what was reported by Brenton-Rule et al. [22] who found the prevalence of fall in RA to range between 10 % – 54 %. The age of fallers was significantly higher than that of non–fallers. This is self-explanatory because of the direct relation between age and both sarcopenia and dynapenia where some authors reported that after the age of 50, there was continuous muscle loss by about 1–2 % per year [27, 28]. The role of the age as a key risk factor of falls was documented in the studies done on the elderly [1, 29] but not on RA patients [23, 30–32].

Disease duration in this study was significantly higher in the fallers than in non-fallers (P value = 0.001). This is contrary to Hayashibara et al. [30] who found no significant differences between fallers and non-fallers in disease duration.

Most of non-fallers (73.2 %) in the current study were having moderate disease activity while 60 % of fallers had high disease activity. The association between high disease activity and fall risk was previously reported [23, 32].

Fallers in the current study showed impaired balance status with high fall risk compared to the non-fallers (P < 0.001). In agreement

▶ **Table 3** Sonographic data of the ankles and feet of the study population.

	Non-fallers (N = 56)	Fallers (N = 45)	P value	Non-fallers (N = 56)	Fallers (N = 45)	P value
		Rt. TTJ			**Lt. TTJ**	
Erosion	10(17.9 %)	6 (13.3 %)	0.368 *	3 (5.4 %)	7 (15.6 %)	0.068 *
G 1	10 (100 %)	3 (50 %)	**0.025 ***	1 (33.3 %)	3 (42.9 %)	0.669 *
G 2	0 (0 %)	2 (33.3 %)		2 (66.7 %)	4 (57.1 %)	
G 3	0 (0 %)	1 (16.7 %)		0	0	
Effusion	2 (3.6 %)	6 (13.3 %)	0.076 *	4 (7.1 %)	3 (6.7 %)	0.621 *
Mild	1 (50 %)	6 (100 %)	**0.037 ** **	3 (75 %)	3 (100 %)	0.553 **
Moderate	1 (50 %)	0 (0 %)		1 (24 %)	0 (0 %)	
SH	13(23.2 %)	16 (35.6 %)	0.137 *	10 (17.9 %)	8 (17.8 %)	0.669 *
G1	5 (38.5 %)	5 (31.2 %)	0.690 *	4 (40 %)	2 (25 %)	0.571 *
G2	6 (46.2 %)	8 (50 %)		5 (50 %)	3 (37.5 %)	
G3	2 (15.3 %)	3 (18.8 %)		1 (10 %)	3 (37.5 %)	
		Rt. TNJ			**Lt. TNJ**	
Erosion	6 (10.7 %)	5 (11.1 %)	0.598 **	6 (10.7 %)	12 (26.7 %)	**0.037 ***
G 1	6 (100 %)	5 (100 %)	0.598 **	5 (83.3 %)	8 (66.7 %)	0.439 **
G 2	0	0		1 (16.7 %)	4 (33.3 %)	
G 3	0	0		0	0	
Effusion	1 (1.8 %)	3 (6.7 %)	0.231 **	1 (1.8 %)	1 (2.2 %)	0.695 **
Mild	0 (0 %)	2 (66.7 %)	0.190 **	0 (0 %)	1 (100 %)	0.247 *
Moderate	1 (100 %)	1 (33.3 %)		1 (100 %)	0 (0 %)	
SH	37 (66.1 %)	31 (68.9 %)	0.476 *	25 (44.6 %)	23 (51.1 %)	0.518 *
G1	21 (56.8 %)	16 (51.6 %)	0.445 *	11 (44 %)	9 (39.1 %)	0.762 *
G2	12 (32.4 %)	9 (29 %)		10 (40 %)	8 (34.8 %)	
G3	4 (10.8 %)	6 (19.4 %)		4 (16 %)	6 (26.1 %)	
PD	1 (1.8 %)	3 (6.7 %)	0.231 **	1 (1.8 %)	2 (4.4 %)	0.418 **
G1	0 (0 %)	2 (66.7 %)	0.190 *	1 (100 %)	2 (100 %)	0.418 **
G2	1 (100 %)	1 (33.3 %)		0	0	
G3	0	0		0	0	
		Rt. 1stMTP			**Lt. 1stMTP**	
Erosion	4 (7.1 %)	4 (9.8 %)	0.514 **	2 (3.6 %)	8 (17.8 %)	**0.020 ** **
G 1	4 (100 %)	4 (100 %)	0.514 **	2 (100 %)	7 (87.5 %)	0.800 **
G 2	0	0		0 (0 %)	1 (12.5 %)	
G 3	0	0		0	0	
Effusion	3 (5.4 %)	5 (11.1 %)	0.243 **	2 (3.6 %)	5 (11.1 %)	0.139 **
Mild	3 (100 %)	5 (100 %)	0.243 **	2 (100 %)	4 (80 %)	0.133 **
Mod.	0	0		0 (0 %)	1 (20 %)	
SH	19 (33.9 %)	20 (44.4 %)	0.191 *	18 (32.1 %)	19 (42.2 %)	0.201 *
G1	7 (36.8 %)	8 (40 %)	0.896 *	4 (22.2 %)	0 (0 %)	0.056 *
G2	8 (42.1 %)	7 (35 %)		7 (38.8 %)	11 (57.9 %)	
G3	4 (21.1 %)	5 (25 %)		7 (38.8 %)	8 (42.1 %)	
PD	3 (5.4 %)	4 (8.9 %)	0.379 **	1 (1.8 %)	4 (8.9 %)	0.121 **
G 1	2 (66.7 %)	2 (50 %)	0.629 **	0	0	0.194 **
G 2	1 (33.3 %)	2 (50 %)		1 (100 %)	3 (75 %)	
G 3	0	0		0 (0 %)	1 (25 %)	
		Rt. 2ndMTP			**Lt. 2ndMTP**	
Erosion	3 (5.4 %)	6 (13.3 %)	0.148 **	0 (0 %)	6 (13.3 %)	**0.006 ** **
G 1	2 (66.7 %)	5 (83.3 %)	0.583 **	0 (0 %)	2 (33.3 %)	**0.001 ** **

▶ **Table 3** Fortsetzung.

	Non-fallers (N = 56)	Fallers (N = 45)	P value	Non-fallers (N = 56)	Fallers (N = 45)	P value
G 2	1 (33.3 %)	1 (16.7 %)		0 (0 %)	4 (66.7 %)	
G 3	0	0		0	0	
Effusion	2 (3.6 %)	4 (8.9 %)	0.241 **	1 (1.8 %)	2 (4.4 %)	0.418 **
Mild	2 (100 %)	4 (100 %)	0.241 **	1 (100 %)	2 (100 %)	0.418 **
Moderate	0	0		0	0	
SH	25 (44.6 %)	18 (40 %)	0.639 *	19 (33.9 %)	13 (28.9 %)	0.373 *
G1	3 (12 %)	2 (11.1 %)	0.789 *	2 (10.5 %)	2 (15.4 %)	
G2	12 (48 %)	11 (61.1 %)		11 (57.9 %)	8 (61.5 %)	0.545 *
G3	10 (40 %)	5 (27.8 %)		6 (31.6 %)	3 (23.1 %)	
PD	2 (3.6 %)	4 (8.9 %)	0.241 **	0 (0 %)	2 (4.4 %)	0.196 **
G1	1 (50 %)	2 (50 %)	0.166 *	0	0	0.201 *
G2	0 (0 %)	2 (50 %)		0 (0 %)	1 (50 %)	
G3	1 (50 %)	0 (0 %)		0 (0 %)	1 (50 %)	
	Rt. Ankle dorsal flexors			**Lt. ankle dorsal flexors**		
Tenosynovitis	12 (21.4 %)	14 (31.1 %)	0.190 *	8 (14.3 %)	14 (31.1 %)	**0.042 ***
Mild	9 (75 %)	9 (64.3 %)	0.492 *	6 (75 %)	10 (71.4 %)	0.180 *
Moderate	3 (25 %)	4 (28.6 %)		2 (25 %)	2 (14.3 %)	
Severe	0 (0 %)	1 (7.1 %)		0 (0 %)	2 (14.3 %)	
PD	1 (1.8 %)	4 (8.9 %)	0.121 **	0 (0 %)	1 (2.2 %)	0.446 **
G1	0 (0 %)	4 (100 %)	**0.020 ** **	0	0	0.446 **
G2	1 (100 %)	0 (0 %)		0 (0 %)	1 (100 %)	
G3	0	0		9	0	
	Rt. ankle planter flexors			**Lt. ankle planter flexors**		
Tenosynovitis	21 (37.5 %)	19 (42.2 %)	0.630 *	18 (32.1 %)	20 (44.4 %)	0.205 *
Mild	12 (57.1 %)	16 (84.2 %)	**0.034 ***	11 (61.1 %)	9 (45 %)	0.260 *
Moderate	7 (33.3 %)	3 (15.8 %)		7 (38.9 %)	10 (50 %)	
Severe	2 (9.6 %)	0 (0 %)		0 (0 %)	1 (5 %)	
PD	1 (1.8 %)	3 (6.7 %)	0.231 **	1 (1.8 %)	2 (4.4 %)	0.231 **
G1	0	0	0.241 *	0 (0 %)	1 (50 %)	0.689 *
G2	1 (100 %)	3 (100 %)		1 (100 %)	0 (0 %)	
G3	0	0		0 (0 %)	1 (50 %)	
	Rt. Peroneal tendons			**Lt. Peroneal tendons**		
Tenosynovitis	22 (39.3 %)	25 (55.6 %)	0.103 *	22 (39.3 %)	20 (44.4 %)	0.374 *
Mild	15 (68.2 %)	20 (80 %)	0.122 *	15 (68.2 %)	12 (60 %)	0.648 *
Moderate	7 (31.8 %)	5 (20 %)		6 (27.1 %)	5 (25 %)	
Severe	0	0		1 (1.8)	3 (15 %)	
PD	2 (3.6 %)	1 (2.2 %)	0.582 *	1 (1.8 %)	2 (4.4 %)	0.231 **
G1	2 (100 %)	0 (0 %)	0.333 *	0 (0 %)	1 (50 %)	0.221 *
G2	0 (0 %)	1 (100 %)		0 (0 %)	1 (50 %)	
G3	0	0		1 (100 %)	0 (0 %)	

* Chi-square analysis was used to compare the frequency among groups. ** Fisher's Exact test was used to compare the frequency among groups. N: number, G: grade, R: right, LT: left, TTJ: tibiotalar joint (ankle joint), SH: synovial hypertrophy, TNJ: Talonavicular joint, MTP: metatarsophalangeal joint, Significance was considered when P value is ≤ 0.05.

▶ **Table 4** Independent Predictors of Falling: Multivariable Logistic Regression.

Factor	OR	95 % CI *	P-value	Predictive Power
Age/years	1.038	1.003–1.074	0.033	58.2 %
Disease Duration/years	1.107	1.037–1.182	0.002	66.3 %
Disease Activity (High)	2.109	1.021–4.254	0.021	61.4 %
Muscle Power				
Weak Rt. Ankle J dorsal flexors & planter flexors.	7.389	2.420–15.741	0.001	68.1 %
Weak Rt. Subtalar Ever. & Inv.	5.628	1.686–11.954	0.002	66.3 %
Weak Lt. Ankle J dorsiflexors & plantar flexors.	3.358	1.168–9.813	0.025	62.4 %
Weak Lt. Subtalar Ever. & Inv.	4.144	1.394–12.727	0.013	63.4 %
Weak Toe Strength	6.193	2.064–18.577	0.001	67.3 %
ROM				
Restricted Rt. Ankle	6.090	2.168–17.108	0.001	68.3 %
Restricted Rt. Subtalar j	9.500	2.929–20.809	< 0.001	70.3 %
Restricted Lt. Ankle	4.385	1.689–11.383	0.002	66.3 %
Restricted Lt. Sub. T	8.833	2.364–23.001	0.001	67.3 %
Foot Type				
Normal	1		0.003	
Flatfoot	5.667	1.415–12.691	0.014	68.3 %
High Arched Foot	8.500	1.713–22.196	0.009	
Ankle & Toe Deformity				
Hammer Toe	3.189	1.129–7.593	0.014	58.1 %
Gait Speed Test (Speed)	0.203	0.069–0.589	0.004	70.3 %
HAQ-DI	1.684	1.032–2.748	0.037	63.4 %
Tinetti Balance Test				
Moderate fall Risk	3.263	1.252–8.499	0.015	69.4 %
Berg Balance Test				
Mild fall Risk	1		< 0.001	
Medium all Risk	3.455	1.286–9.289	0.014	71.3 %
High fall Risk	16.00	6.889–38.126	< 0.001	
Sonographic Data				
Lt. TNJ Erosion	3.030	1.035–8.870	0.043	61.4 %
Lt. 1st MTP Erosion	5.838	1.173–19.059	0.031	62.6 %
Lt. Extensor Tenosynovitis	2.710	1.018–7.213	0.046	55.2 %

* OR = Odds Ratio, CI = Confidence Interval. Rt: right, Lt: Left; Ever: Evertors, Inv: Invertors, HAQ-DI: Health assessment questionnaire-disability index, TNJ: Talonavicular joint; MTP: Metatarsophalangeal, Significance was considered when P value is ≤ 0.05

with this finding, Rome et al. [33] reported that patients with RA experience difficulty in posture controlling during performing activities of daily livings compared to healthy population.

Higher disability index was reported among the faller group in this study compared to non-fallers group (P = 0.009). Functional disability detected by HAQ-DI was previously delineated by many investigators as a fall risk factor in RA patients [2, 34, 35].

The speed of the faller's gait was significantly slower than that of the non-fallers (P value < 0.001). This is in concordance with Lusa et al. [36] who found that RA patients had low mean gait speed and reported several contributing factors including older age, high swollen joint count, depression, high prednisone dose and non-treatment with diseases modifying drugs. Furthermore, Fallers and non-fallers in this study had median gait speed value lower than 1.4 m/sec which is required speed for independent outdoor ambulation [37]. This gives the impression that all RA patients are at risk of falling whether they had experienced previous fall or not.

As regards the clinical examination of foot and ankle, feet of the fallers in the current study showed more muscle weakness, restricted ROM than those of non-fallers. The association between musculoskeletal problems and fall risk was reported by several population-based studies [38–40]. Nearly the same was reports in patients with RA where muscle weakness and joint pain and stiffness were found to be considerable risk factors of falls [34, 41].

▶ **Table 5** Sensitivity and specificity of Different fall predictors in the study population.

	AUC	Accuracy	Sensitivity	Specificity	PPV	NPV
Clinical Finding						
Disease Duration (7.5 y)	0.690	70 %	72 %	67 %	69 %	71 %
Muscle Power						
Weak Rt. Ankle dorsal flexors & planter flexors	0.653	63 %	65 %	61 %	62.5 %	63.5 %
Weak Rt. Subtalar Ever. & Inv.	0.633	62.5 %	67 %	58 %	61.5 %	64 %
Weak Toe Strength	0.644	68.5 %	72 %	65 %	67 %	70 %
ROM						
Restricted Rt. Ankle	0.658	71 %	77 %	65 %	69 %	74 %
Restricted Rt. Subtalar	0.675	83 %	87 %	73 %	75.5 %	81 %
Restricted Lt. Ankle	0.640	65 %	69 %	61 %	64 %	66 %
Restricted Lt. Subtalar	0.640	65 %	69 %	61 %	64 %	66 %
Ankle and Foot Characters						
Foot Type	0.657	72.5 %	79 %	66 %	70 %	76 %
Hammer Toe	0.619	63.5 %	68 %	59 %	62 %	65 %
Diagnostic Scales and Questionnaires						
Gait Speed Test	0.748	70 %	73 %	67 %	69 %	71 %
HAQ-DI	0.653	62 %	62 %	62.5 %	62 %	62 %
Tinetti balance test	0.778	70.5 %	80 %	61 %	67 %	75 %
Berg balance test	0.786	84 %	89 %	79 %	81 %	88 %
Sonographic Parameters						
Lt. TNJ Erosion	0.642	70.5 %	77 %	64 %	68 %	73.5 %
Lt. 1st MTP Erosion	0.656	72.5 %	75 %	70 %	71.5 %	73.5 %
Lt. Extensor tenosynovitis	0.614	64 %	66 %	62 %	63.5 %	64.5 %

* Sensitivity (true positives/all diseased); specificity (true negatives/all non-diseased); PPV (true positives/all test positives); NPV (true negatives/all test negatives). AUC: area under curve, PPV: Positive predictive value, NPV: Negative predictive value; Rt: right. Lt: Left, Ever: Evertors, Inv: Invertors, HAQ-DI: Health assessment questionnaire-disability index, TNJ: Talonavicular joint; MTP: Metatarsophalageal joint

In the current study, there were significant differences between the fallers and non- fallers as regards the erosion of the 1st MTP, 2nd MTP, and talonavicular joint (TNJ) in addition to effusion of the ankle joint. Furthermore, tenosynovitis were found to be significantly different between the 2 groups on the level of the ankle plantar flexors and dorsal flexors but not on the level of peroneal tendons.

As regards joint changes in this study, synovial hypertrophy of the TNJ was the most common finding. The number of affected TNJ in the non-fallers was higher than that in fallers, similar finding was detected at the level of 2nd MTP joint. This could be due to the high ability of MSUS to detect subclinical synovitis even in asymptomatic joint. In agreement with our findings, the cross sectional study of Petterle et al. [42] who demonstrated that ultrasonography could detect subclinical changes in asymptomatic ankles and feet in both RA and healthy control groups and that the TNJ was the most affected joint.

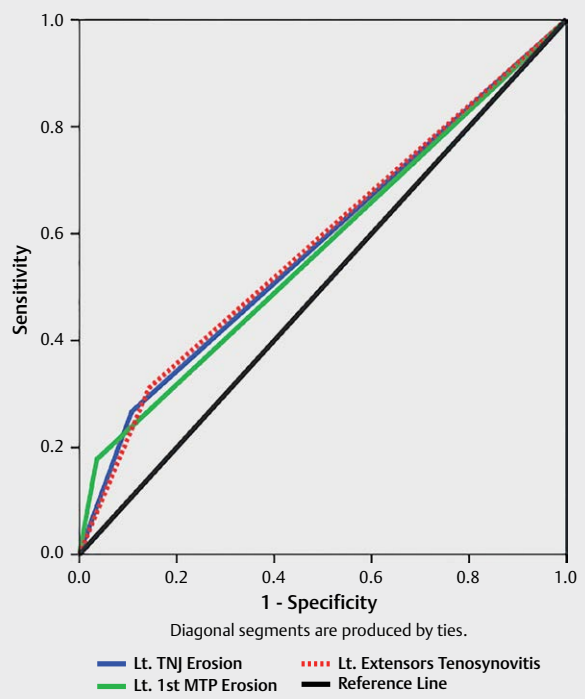
Regarding tendon abnormality, tenosynovitis of the peroneal tendons in the study population was the most common sonographic finding. In accordance with our finding, Lehtinen et al. [43] reported that ankle and subtalar synovitis were the commonest joints abnormality detected followed by peroneal tenosynovitis.

Using the multiple regression analysis, we found that the most predictive factor of fall was the Berg balance scale (BBS) with predictive power of (71.3 %), followed by gait speed and restricted subtalar ROM with predictive power of (70.3 %) each.

In contrast to our findings, Lima et al. [44] in their systematic review found conflicting results as regards the cutoff point of BBS and recommended against its use as a fall predictor.

Slow gait was a well-documented, definite predicting factor of falls, functional limitation and mortality in older people. Van Kan et al. concluded that gait speed in normal pace can be used as a single item assessment tool of adverse outcomes including falls [45]. But this was not proved in RA, where some authors postulated that slow gait speed in RA is protective against falling and that RA patients preferred a slower gait speed than that of the controls [46].

From all the sonographic features reported in this study, erosion of 1st MTP joint, erosion of the TNJ and ankle's extensors tenosynovitis were found to be the predictors of falls in our studied population with predictive power of (62.6 %, 61.4 % and 55.2 %) respec-



▶ **Fig. 1** Receiver operating characteristic (ROC) curve of Sonographic findings as Falling Predictorsin RA patients. **Lt.** Left, **TNJ** Talonavicular joint, **MTP** metatarsophalangeal joint, **Extensor tenosynovitis** dorsiflexors tenosynovitis..

tively. One study (22) investigated the role of foot pathology as a predictor of fall in RA patients and concluded that midfoot derangement including the TNJ and self- reported foot deformity were the predictors.

Sonographic assessment of the 1st MTP joint was included in this study because the role of mechanical forces in the development of foot pathology in RA patients cannot be rolled out [47]. Ultrasonography investigators had postulated that the initial synovitis of the MTP joints occurring early in RA is followed and augmented by mechanical loads, and both factors are incorporated in the development of MTP joint pathology in RA [48].

On using ROC curve to study the sensitivity and specificity of the previously detected predictors, Berg balance scale (BBS), Tinetti balance test and gait speed test were the most accurate predictors with area under curve (AUC) of (0.786, 0.778 and 0.748) respectively. Among the three aforementioned sonographic predictors, erosion at the 1st MTP joint was the most accurate predictor of falls with AUC of (0.656), sensitivity of (75 %) and specificity of (70 %). Foot and ankle MSUS failed to show superiority over the clinical tests in predicting falls in RA patients.

To our knowledge, this is the first study to investigate the ankles and feet MSUS changes as a predictors of falls in RA patients. This study has some limitations including the questioned inter observer reliability of the sonographic examination, the cross sectional nature of the study and the small study sample. A Larger scale longitudinal study is recommended to confirm the present results and investigate more fall predictors.

Conclusion

In conclusion, depending on the results of the present study, there was no justified clue to use the MSUS as a prediction tool in RA patients and the clinical balance tests as Berg balance scale (BBS), Tinetti balance test and gait speed test maintain their upper hand as fall predictors.

Contributor's Statement

Eman A M Alkady: Administration, Supervision, Validation and review & editing.
Marwa Mahmoud Abdelaziz: Drafting of the submitted protocol and critical revision of the submitted protocol for important intellectual content, Revision
Dalia Abdelwahed: Acquisition of data, Analysis and interpretation of data, Statistical analysis
Safaa Ali Mahran: Conception and design, Critical revision of the submitted protocol for important intellectual content, and writing the manuscript.

Conflict of interest

The authors declare that they have no conflicts of interest.

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